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09/996,263	11/28/2001	Phillip Dan Cook	ISIS-4943	3783

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EXAMINER

SCHULTZ, JAMES

ART UNIT PAPER NUMBER

1635

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/996,263
Filing Date: November 28, 2001
Appellant(s): COOK ET AL.

Jeffrey H. Rosedale
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 5, 2004.

(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct. However, Appellants' indication of the specification's support for the invention is disagreed with, and is discussed further under the section entitled "Arguments".

(6) *Issues*

The appellant's statement of the issues in the brief is substantially correct. However, the rejection under 35 U.S.C. § 112 first paragraph for lacking written description is hereby withdrawn. Importantly, Appellants had also been denied priority to any earlier parent application based on reasoning set forth in the rejection under 35 U.S.C. § 112 first paragraph written description, and this denial of priority is maintained. Accordingly, the rejection under 35 U.S.C. § 102(b) is also maintained, and is discussed further in the "arguments" section.

(7) *Grouping of Claims*

The brief provides a statement that the claims stand or fall together.

(8) *Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) *Prior Art of Record*

5612215

Draper et al.

03-1997

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 8-13 stand finally rejected under 35 U.S.C. 102(b) as being anticipated by Draper et al. (U.S. Patent Number 5,612,215).

The invention of the above listed claims is drawn to a mixed sequence oligonucleotide or oligonucleotide analog including more than one 2'-modified 2'-deoxyfuranosyl moiety wherein said modification comprises substitution by halo, azido, amino, alkoxy, thioalkoxy, alkylamino, alkyl, and wherein one of said 2'-modified 2'-deoxyfuranosyl moieties is different from another of said 2'-modified 2'-deoxyfuranosyl moieties, or wherein one of the two different moieties is alkoxy, which may be methoxy, or an alkyl group which may comprise a straight or branched chain alkyl, wherein said alkyl may be unsaturated, and said nucleotide sequence that is nuclease resistant.

The oligos of Draper et al. comprise phosphorothioated nucleotides sequences containing both 2'-O-methyl moieties, and 2'-C-allyl modifications (see claim 20), thus meeting all the limitations of all pending claims.

Draper is considered to be applicable as prior art under 35 U.S.C. § 102(b) because claims 8-13 have not been accorded priority to any earlier application. Appellants' claim of priority extends back via numerous continuations, divisionals, and continuations-in-part, but discussion has centered upon an exemplary U.S. Application, Number 07/835,932 (the "932" application) to which appellants argue provides support, and that pre-dates the filing date of the

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Draper reference. Priority has been denied because neither the 932 application nor any of the related applications, are considered to disclose all the limitations of the instant claims, and are thus not considered to provide adequate support for a priority claim to an earlier application. The limitations that are considered to be absent in previous teachings pertain to oligonucleotides containing more than one nucleotide modification wherein said modifications are different from each other, and are chosen from a Markush group of modifications.

The teachings of the earlier specifications to which appellants claim priority are not considered to support the instant claims drawn to oligos containing two or more different modifications chosen from a broad list of modifications because no teaching can be found that directs one of skill to these requirements, with one exception. However, this exception is not considered to provide adequate support for claims to the broad classes of modifications now being claimed. Said exception pertains to a single combination of 2'-methythio and 2'-O-methyl modifications taught on page 64 of U.S. Application Number 08/471,973. While it is granted that this combination falls within the scope of the instant claims, there are several reasons why said combination is not considered to provide adequate support for any oligo containing two or more different modifications chosen from the broad list now claimed.

The first reason the prior applications lack support is that the single combination of 2'-methythio and 2'-O-methyl modifications is apparently the lone reference to any oligo that contains two or more different modifications from any of the 13 parent documents. Other than this single combination, the examiner has not found, nor have appellants pointed to, any teaching anywhere by way of prophetic statement, assertion, or exemplification that an oligo comprising

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two or more different modifications chosen from the broad list claimed instantly was ever contemplated by the inventors.

Furthermore, the context in which the lone combination appears is silent as to any indication that such dually modified oligos are considered to be advantageous, or are a goal of the invention, or are in any other way desirable. All that is taught therein is that the oligos were made.

Finally, the lone combination that falls within the scope of the instant claims is not considered representative of the breadth instantly claimed. The single combination of an oligo comprising 2'-methythio and 2'-O-methyl modifications is not considered to lead one of skill to any oligo containing at least two different modifications chosen from the list including halo, azido, amino, alkoxy, thioalkoxy, alkylamino, alkyl, particularly in view of the absence of any contextual description or support indicating that the inventor envisioned such oligos containing two different such modifications.

(11) *Response to Argument*

As stated above, claims 8-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Draper et al. (U.S. Patent Number 5,612,215). Appellants have not provided any arguments denying that the Draper reference teaches all the claim limitations. Rather, Appellants argue that the Draper reference is not a proper reference under 35 U.S.C. § 102(b), because Appellants argue they are entitled to an earlier filing date. Accordingly, the issue at hand is whether Appellants can antedate the Draper reference by pointing to adequate support contained in any earlier application to which priority is claimed for the instant limitations pertaining to more than

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one nucleotide modification wherein said modifications are different from each other, and are chosen from a Markush group of modifications.

As a preliminary matter, it is important to note that the rejection under 35 U.S.C. § 112 first paragraph for lacking written description has been presently withdrawn. However, the rationale for denying priority is based on the same analysis, and said rationale continues to be relied upon in denying priority to the parent documents. That rationale is simply that adequate support is not considered to exist in any earlier application to which priority is claimed for the instant limitations pertaining to more than one nucleotide modification (which are chosen from a Markush group of broad modifications) wherein said modifications are different from each other.

The reason that the instant rejection under 35 U.S.C. § 112 first paragraph written description has been withdrawn is that although not pointed out by appellants, the two critical limitations now claimed (i.e. two different modifications on the same oligo) were recited in the claims as originally filed, and are thus in fact a part of the present specification. However, no previous application teaches the instantly claimed requirements for two or more modifications that are different from each other, and thus, the denial of priority to any earlier application is maintained.

As stated above, the teachings of the earlier specifications to which appellants claim priority are not considered to support the instant claims drawn to oligos containing two or more different modifications chosen from a broad list of modifications because no teaching can be found that directs one of skill to these requirements, with the one exception discussed above.

Appellants have argued that the single combination of an oligo comprising 2'-methythio and 2'-O-methyl modifications actually provides adequate description for claims directed to any

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oligo containing at least two different modifications chosen from the list including halo, azido, amino, alkoxy, thioalkoxy, alkylamino, alkyl. For reasons discussed above in the “Grounds of Rejection” section, these arguments are not considered convincing. To reiterate, the oligo discussed above is not considered to lead one of skill in the art to any oligo containing at least two different modifications, because nowhere beyond the single combination of modifications taught does it so much as mention that two different modifications in general are considered to be encompassed or desirable, and also because the lone combination taught is not representative of the breadth now claimed.

Appellants have also argued that “Oligonucleotides suited for the practice of the present inventions generally comprise more than one 2'-modified nucleotide wherein the 2'-modifications are with different substituents” and point to page 10, line 27 to page 11, line 4 for support, where it states in its entirety:

“It is desired that the oligonucleotides of the invention be adapted to be specifically hybridizable with the nucleotide sequence of the target RNA or DNA selected for modulation. **Oligonucleotides particularly suited for the practice of one or more embodiments of the present invention comprise 2'-sugar modified oligonucleotides wherein one or more of the 2'-deoxy ribofuranosyl moieties of the nucleoside is modified with a halo, alkoxy, aminoalkoxy, alkyl, azido, or amino group.** For example, the substitutions which may occur include F, CN, CF₃, OCF₃, OCN, O-alkyl, S-alkyl, SMe, SO₂, Me, ONO₂, NO₂, NH₃, NH₂, NH-alkyl, OCH₃=CH₂ and OCCH. In each of these, alkyl is a straight or branched chain of C1 to C20, having unsaturation within the carbon chain. A preferred alkyl group is C1-C9 alkyl. A further preferred alkyl group is C5-C20 alkyl.” (bold added)

As can be seen above, nowhere does this passage indicate that the modifications must comprise two or more different modifications, which stands in contrast to appellants' assertion that the invention “generally comprise more than one 2'-modified nucleotide wherein the 2'-modifications are with different substituents”. In fact, it is maintained that because the list is presented in the alternative, the only proper interpretation that can be made is that there may be

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more than one nucleotide on a given oligo that may be modified, but that all modifications are the same. Accordingly, Appellants' view that the instant invention "generally comprise more than one 2'-modified nucleotide wherein the 2'- modifications are with different substituents" is not considered to be consistent with the teachings of the priority document, and priority has thus been denied.

Appellants have alleged that the examiner did not meet the burden of establishing a *prima facie* case of lack of written description. However, keeping in mind that the rejection is based on a deficiency in the specification, it is unclear what evidence could be produced that something in the specification is missing, other than to point out that there is a deficiency in the specification. The examiner was unable to locate any specific teachings pertaining to the limitations of two or more different modifications in any priority documents. Accordingly, appellants were invited to point to any such specific teachings, and have not yet done so.

Appellants also allege that the declaration under CFR § 1.132 has not been fully considered and rebutted. This is disagreed with. Although the declaration was submitted after final and thus after prosecution had been closed, the declaration was considered and responded to in an after final communication. Appellants allege that the examiner failed to analyze or substantively discuss the declaration, and further failed to identify contrary evidence or some identifying deficiency in the declaration. This is not considered to be accurate for the following reasons.

The declaration was responded to by pointing out that the examiner had not been able to locate, and neither the declaration nor applicants arguments pointed to, any teaching beyond the one exemplified oligo that would lead one of skill to make any other oligo that must contain at

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least two different modifications chosen from said broad list. This was considered to be particularly true because although the specification does teach the one exemplified oligo, there is no mention that this one combination is desirable or useful in any way, let alone that other combinations may be desirable or useful. It was further pointed out that the lists of modifications pointed to by appellants to support their arguments appear directed only to oligos containing one type of modification, because the list specifically recites the alternative language "or", which would lead one of skill to interpret that the modifications were not contemplated as useful together.

Finally it was submitted in the after final communication that the mere listing of numerous modifications does not stand as evidence that they were contemplated as being used in combination on the same oligo. Here too, applicants have pointed to no mention or suggestion that two or more modifications on the same oligo were ever contemplated beyond the narrow embodiment disclosed in example 13.

Thus, the arguments of the declaration are considered to be responded to in full, particularly in view of the fact that the affidavit submitted after final does not contain any evidence of written description, but rather merely sets forth opinions on what is essentially a fact-based inquiry.

For the above reasons, it is believed that the rejection should be sustained.

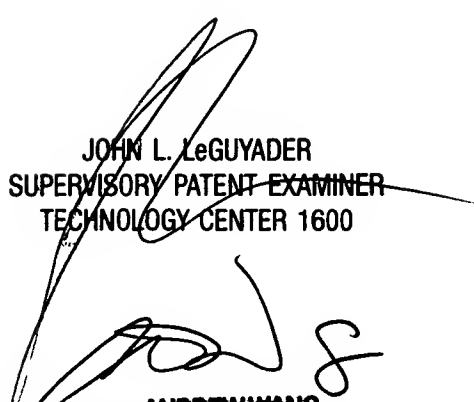
Respectfully submitted,

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July 23, 2004

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